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My Summer Refuge

Donna Kunkel

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About the cover

My Summer Refuge was painted by Donna Kunkel, wife of Dr. John Kunkel, an extension veterinarian at the University of Vermont. Her works have been featured in solo and group exhibits and appear in private collections throughout the country.

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VBPA

Locations and types of neoplasms in immature dogs: 69 cases (1964–1989)

Evan T. Keller, DVM, MPVM, and Bruce R. Madewell, VMD, MS

Summary: *Sites, histologic types, and frequencies of neoplasms in immature dogs (≤6 months old) were evaluated from data collected over 25 years. The frequencies of neoplasms in immature dogs were compared with those of mature dogs (>6 months old).*

Of 69 immature dogs with neoplasms, 5 had 2 primary neoplasms each, resulting in a total of 74 neoplasms. The 3 most common sites for neoplasia, in decreasing order, were the hematopoietic system, brain, and skin. Immature dogs were 10.9 times more likely to have a neoplasm located in the brain, compared with mature dogs. Immature dogs also were 3.3 times more likely to have a neoplasm associated with the hematopoietic system, compared with mature dogs.

In human beings, the predominant type of neoplasm observed varies according to age group. Neoplasms derived from the hematopoietic system, thyroid gland, testis, and CNS are most prevalent in human beings <29 years old, whereas neoplasms derived from the urinary bladder, colon, and lungs are most prevalent in human beings 50 to 59 years old.[1] Leukemias and neuroblastoma are the most frequently diagnosed fatal neoplastic diseases in children <1 year old.[2]

Few studies have focused on neoplasia in immature dogs. Mulvihill and Priester[3] have reported that the histiocytoma was the most prevalent tumor in dogs <2 years old, and affected dogs were at greatest risk between 6 and 12 months of age. In that study, only 3 tumors were identified in dogs <3 months old; thus, evaluation of tumor location was not done. Data of tumors from records that were derived from schools and colleges of veterinary medicine in the United States and Canada from 1968 through 1979 listed 17,435 microscopically confirmed tumors in dogs, of which 395 were in dogs <1 year old.[4] The tumor data were not categorized to allow examination of specific types or preference sites in immature dogs.

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The purposes of the study reported here were to determine the types and locations of neoplasms in immature dogs, and to determine estimates of risk for particular neoplasms in immature vs mature dogs with neoplasia.

Criteria for Selection of Cases

Summaries of medical records of dogs ≤6 months old with neoplasia were obtained from data contributed to the Veterinary Medical Data Program (VMDP)[a] between March 1, 1964 and July 1, 1989. Cases were excluded if complete data regarding age of dog or type of neoplasm confirmed histologically were not available.

Data for mature dogs (>6 months) were derived by retabulation of data from an earlier study of the VMDP which only examined data from dogs between March 1, 1964 and June 30, 1977.[4] Thus, only records from immature dogs of the same period as those of the mature dogs were used for statistical comparison.

Statistical analysis

For each tumor site, odds ratios with 95% confidence intervals were generated.[5] Odds ratios were calculated by dividing the ratio of tumors found at a particular site in immature dogs by that in mature dogs. Significance was determined at $P \leq 0.05$. Odds ratios for hemangiosarcoma locations were not determined, because the tumor was found at numerous sites. Locations for this tumor were included in the data from mature dogs.

Results

Of 73 dogs <6 months old with histologically confirmed neoplasms, 4 were excluded because of incomplete data. Of the remaining 69 dogs, 5 had 2 primary tumors each. These dogs included 20 sexually intact females, 10 spayed females, 35 sexually intact males, 3 castrated males, and 1 unknown. Estimates of risk for all gender categories were not significantly different. The most common breeds identified were mixed breed (n = 20),

[a]Veterinary Medical Data Program; a repository for veterinary medical data located at Purdue University, West Lafayette, Ind.

Golden Retriever (n = 8), German Shepherd Dog (n = 7), Doberman Pinscher (n = 5), and Great Dane (n = 4).

The hematopoietic system, brain, and skin (in decreasing order) were the most frequently affected sites (Fig 1). When records for only those immature dogs with tumors identified between March 1, 1964 and June 30, 1977 were selected, 26 dogs were identified and 2 of them had 2 primary tumors each. The data from these 26 immature dogs were compared with the data from the mature dogs (Table 1). The brain and the hematopoietic system were the only 2 sites in the immature dog with significantly increased estimates of risk.

Data from breeds of dogs known to be at risk for specific neoplasms were examined. At least 4 of 5 immature dogs with osteogenic sarcoma were large-breed dogs, and 2 of 4 immature dogs with intranasal neoplasms had dolichocephalic skull conformation.

Discussion

Several confounding factors should be accounted for in interpreting the study. A true sampling of the canine population to develop estimates of risk for neoplasia is difficult to accomplish, especially for neonates. Most young dogs with neoplasms probably die without veterinary involvement. The VMDP represents only referred animals, and may not represent the true spectrum of tumors seen in private practice. Finally, coding of data was not validated, thus coding errors could affect the results of this study. Estimates of risk were based on our study population of dogs that all had neoplasia, and, thus, reflect proportional morbidity.

The brain and hematopoietic system are sites of high risk for cancer in human infants.[1,2,6,b] Of the 74 neoplasms identified in immature dogs of our study, 15 were from the hematopoietic system. It is known that risk for malignant lymphoma increases with age. The age-specific incidence for dogs <1 year old was estimated at 1.5/100,000 dogs/yr, with an increase to 84/100,000 in the 10- to 11-year-old group.[7] According to our data in dogs, the risk for lymphoma was greater in dogs ≤6 months old than dogs >6 months old. Thus, a bimodal peak for lymphoma in dogs may exist that is analogous with the bimodal peaks in human beings for 2 hematopoietic tumors, namely acute lymphocytic leukemia and Hodgkin's disease.[8] Specific causes or risk factors have not been identified for hematopoietic neoplasms in immature dogs, but cellular transmission of malignant lymphoma has been accomplished experimentally in irradiated and nonirradiated neonates, which may indicate that it is infectious.[9-12] Genetic factors may influence the risk for malignant lymphoma in

[b]Barson AJ. Congenital neoplasia: the society's experience (abstr). *Arch Dis Child* 1978;54:436.

Site	No.
Hematopoietic system	15
Lymphoma (12)	
Lymphoid Leukemia (1)	
Granulocytic leukemia (1)	
Multiple myeloma (1)	
Brain	11
Meningioma (4)	
Glioma (2)	
Hamartoma (1)	
Lipoma (1)	
Astrocytoma (1)	
Ependymoma (1)	
Choroid plexus papilloma (1)	
Skin	8
Mastocytoma (3)	
Papilloma (1)	
Melanoma (1)	
Histiocytoma (1)	
Hamartoma (1)	
Lymphangiosarcoma (1)	
Endocrine System	6
Pancreatic islet cell carcinoma (5)	
Pheochromocytoma (1)	
Bone	6
Osteosarcoma (5)	
Osteoma (1)	
Oral Cavity	5
Ameloblastoma (1)	
Basal cell carcinoma (1)	
Melanoma (1)	
Papillomatosis (1)	
Squamous cell carcinoma (1)	
Genitourinary tract	5
Bladder transitional cell carcinoma (1)	
Nephroblastoma (1)	
Transmissible venereal tumor (1)	
Testicular seminoma (1)	
Interstitial cell tumor (1)	
Nasal Cavity	4
Squamous cell carcinoma (2)	
Adenocarcinoma (1)	
Chondrosarcoma (1)	
Respiratory Tract	4
Adenocarcinoma (3)	
Chondrosarcoma (1)	
Miscellaneous	10
Leiomyosarcoma intestinal (1)	
Nodular ganglioneuroma (1)	
Sarcoma (1)	
Fibroma spinal cord (1)	
Hemangiosarcoma (6)	
Total tumors	74

Figure 1—Sites and frequencies of 74 neoplasms in 69 dogs <6 months old (data collected from March 1964 to June 1989).

Table 1—Odds ratios, with 95% confidence intervals, for site of neoplasm for immature vs mature dogs from data collected between Feb 28, 1964 and July 1, 1977.

Tumor site	Immature dogs	Mature dogs*	Odds ratio	95% Confidence interval
Brain	5	339	10.9	[4.1 to 28.9]†
Hematopoietic system	8	1,907	3.3	[1.4 to 7.4]†
Respiratory tract	1	235	2.7	[0.4 to 20.0]
Endocrine system	2	725	1.8	[0.4 to 7.5]
Oral cavity	2	1,108	1.1	[0.3 to 4.8]
Genitourinary tract	2	1,542	0.8	[0.2 to 3.3]
Bone	1	1,119	0.5	[0.1 to 4.1]
Skin	3	3,572	0.5	[0.1 to 1.5]
Miscellaneous	4	6,860	NA	NA
Total	28	17,407	NA	NA

*Data from Priester et al.[4] †Indicates significance ($P = 0.05$).
NA = Not available.

dogs because a high risk for this neoplasm had been identified in some families of English Bullmastiffs.[13]

In our study, the second most frequently recognized site for neoplasia was the brain (n = 11). In human beings, brain tumors constitute the most common type of solid malignancy in children[14] whereas dogs have increased risk with age for all nervous-system tumors.[15] Some perinatal events can induce neoplasia of the CNS in dogs. Intracranial gliomas and sarcomas have been induced in puppies within several weeks of in utero injection with Rous sarcoma virus,[16] and exposure to radiation perinatally has been associated with an astrocytoma in a 3-month-old dog.[17]

Osteogenic sarcomas were found primarily in large-breed dogs, and half of the immature dogs with intranasal neoplasms had dolichocephalic skull conformation. These data were consistent with other studies.[18,19] Other breed and tumor associations were not found, possibly because of the small sample size, or because the factors that influenced risk for neoplasia within a specific breed of dog are not manifested until late in life.

The similarities of sites affected with neoplasms between the human infant and the immature dog may indicate a susceptibility of these tissues to carcinogenic influences in the perinatal period. Dogs closely share our environment, and perhaps neoplasms derived from the brain or hematopoietic tissues in immature dogs are influenced by the same events that influence development of neoplasms in human beings.

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